

WHAT IS CLAIMED IS:

1. A method of characterizing the biological activity of a candidate compound comprising:

exposing one or more cells to said compound;

repetitively exposing said one or more cells to one or more electric fields so as to effect a controlled change in transmembrane potential of said one or more cells; and

monitoring, without using a patch clamp, changes in the transmembrane potential of said one or more cells.

- 2. The method of Claim 1, wherein said monitoring comprises detecting fluorescence emission from an area of observation containing said one or more cells.
 - 3. The method of Claim 1, wherein said electric fields are biphasic.
- 4. The method of Claim 3, additionally comprising limiting spatial variation in electric field intensity so as to minimize irreversible cell electroporation.
- 5. The method of Claim 1, wherein one or more electrical fields cause an ion channel of interest to cycle between different voltage dependent states.
- 6. The method of Claim 5, wherein said one or more electrical fields cause an ion channel of interest to open.
- 7. The method of Claim 5, wherein said one or more electrical fields cause an ion channel of interest to be released from inactivation.
- 8. The method of Claim 1, wherein said one or more cells comprise a voltage sensor selected from the group consisting of a FRET based voltage sensor, an electrochromic transmembrane potential dye, a transmembrane potential redistribution dye, an ion sensitive fluorescent or luminescent molecule and a radioactive ion.
- 9. The method of Claim 1, wherein said one or more cells comprise a voltage regulated ion channel.
- 10. The method of Claim 9, wherein said voltage regulated ion channel is selected from the group consisting of a potassium channel, a calcium channel, a chloride channel and a sodium channel.

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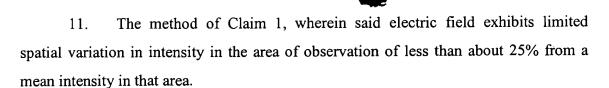
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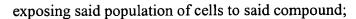


- 12. The method of Claim 11, wherein said one or more electrical fields varies over an area of observation by no more than about 15 % from the mean electrical field at any one time.
- 13. The method of Claim 12, wherein said one or more electrical fields varies over an area of observation by no more than about 5 % from the mean electrical field at any one time.
- 14. The method of Claim 1, wherein said one or more electrical fields comprises stimulation with either a square wave-form, a sinusoidal wave-form or a saw tooth wave-form.
- 15. The method of Claim 1, wherein said one or more electrical fields have an amplitude within the range of about 10 V/cm to about 100 V/cm.
- 16. The method of Claim 15, wherein said one or more electrical fields have an amplitude within the range of about 20 V/cm to about 80 V/cm.
- 17. The method of Claim 1, wherein said one or more electrical fields are repeated at a frequency of stimulation that is greater than or equal to the reciprocal of the transmembrane time constant of said one or more cells.
- 18. The method of Claim 1, wherein said one or more electrical fields are repeated at a frequency of stimulation within the range of zero to 1kHz.
- 19. The method of Claim 1, wherein said one or more electrical fields have a pulse duration within the range of about 100 microseconds to about 20 milliseconds.
- 20. The method of Claim 1, wherein said transmembrane potential is developed across the plasma membrane of said one or more cells.
- 21. A method of assaying the biochemical activity of a compound against a target ion channel comprising:

selecting a cell line having a normal resting transmembrane potential corresponding to a selected voltage dependent state of said target ion channel;

expressing said target ion channel in a population of cells of said selected cell line;

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repetitively exposing said population of cells to one or more electric fields so as to effect a controlled change in transmembrane potential of said one or more cells; and

monitoring changes in the transmembrane potential of said one or more cells.

- 22. The method of Claim 21, wherein said target ion channel is exogenously expressed in said cell line.
- 23. The method of Claim 21, wherein said cell line is transfected with nucleic acid encoding said target ion channel.
- 24. The method of Claim 23, wherein said cell line expresses insignificant levels of other ion channels.
- 25. The method of Claim 24, wherein said cell line is selected from the group consisting of CHL, LTK(-), and CHO-K1.
- 26. The method of Claim 21 wherein said target ion channel is a sodium channel, and wherein said population of cells is selected from the group consisting of CHL cells, LTK(-) cells, and CHO-K1 cells.
- 27. The method of Claim 21 wherein said target ion channel is a sodium channel, and wherein said population of cells is selected from the group consisting of HEK-293 cells, RBL cells, F11 cells, and HL5 cells.
- 28. The method of Claim 21 wherein said target ion channel is a potassium channel, and wherein said population of cells is selected from the group consisting of CHL cells, LTK(-) cells, and CHO-K1 cells.
- 29. The method of Claim 21 wherein said target ion channel is a calcium channel, and wherein said population of cells is selected from the group consisting of CHL cells, LTK(-) cells, and CHO-K1 cells.
 - 30. A method of assaying ion channel activity comprising:

exposing at least one cell to a plurality of electric field pulses so as to create a controlled change in transmembrane potential and so as to activate an ion channel of interest, and

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detecting ion channel activity by detecting one or more changes in transmembrane potential without using a patch clamp.

- 31. The method of claim 30, wherein said at least one cell comprises a voltage sensor selected from the group consisting of a FRET based voltage sensor, an electrochromic transmembrane potential dye, a transmembrane potential redistribution dye, an ion sensitive fluorescent or luminescent molecule and a radioactive ion.
- 32. The method of Claim 31 wherein said voltage sensor comprises a FRET based voltage sensor.
- 33. The method of Claim 32, wherein said ion channel of interest is a voltage regulated ion channel.
- 34. The method of Claim 33, wherein said plurality of electric field pulses cause said ion channel of interest to cycle between different voltage dependent states.
- 35. The method of Claim 30, wherein said at least one cell is an eukaryotic cell.
- 36. The method of Claim 30, wherein said at least one cell is a non-excitable cell.
- 37. The method of Claim 30, wherein said at least one cell is a prokaryotic cell.
- 38. The method of Claim 30, wherein said at least one cell is a tissue culture cell.
- 39. The method of Claim 30, wherein said at least one cell is a primary cell line.
- 40. The method of Claim 30, wherein said at least one cell is part of an intact living organism.
- 41. A method of assaying ion channel activity comprising:
 expressing a selected target ion channel in at least one cell;
 expressing a selected counter ion channel in said at least one cell;

exposing said at least one cell to a plurality of electric field pulses so as to create a controlled change in transmembrane potential and so as to activate said counter ion channel; and

monitoring the transmembrane potential of said at least one cell.

- 42. The method of Claim 41, wherein a transmembrane potential change is detected when said ion channel of interest is blocked.
- 43. The method of Claim 42, wherein said ion channel of interest comprises a ligand gated ion channel.
- 44. The method of Claim 43, wherein said counter channel comprises a sodium channel.
- 45. A method of modifying the transmembrane potential of a cell comprising repetitively applying biphasic electric field pulses to said cell, wherein said pulses have a maximum amplitude of less than approximately 90 V/cm, wherein said pulses are applied at a rate of at least about 1 per second, and wherein the total duration of each pulse is at least about 1 millisecond.
- 46. The method of Claim 45, wherein said maximum amplitude is approximately 20 to 40 V/cm.
- 47. The method of Claim 45, wherein said pulse duration is approximately 2 to 10 milliseconds per phase.
- 48. The method of Claim 45, wherein said pulses are applied at a rate of approximately 20 to 100 pulses per second.

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